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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	22

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/117,357	Applicant(s) STOCKMANN et al.
	Examiner Cybille Delacroix-Muirheid	Art Unit 1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 30, 2001 and Oct. 30, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *11-14, 20, 30, 33-36, 40, and 42-52* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *11-14, 20, 30, 33-36, 40, and 42-47* is/are allowed.

6) ☒ Claim(s) *48-52* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

The following is responsive to the Supplemental amendment received Jul. 30, 2001 and the amendment received Oct. 30, 2001.

In the amendment received Jul. 30, 2001, new claims 44-50 are added. In the amendment received Oct. 30, 2001 new claims 51-52 are added and claims 15, 16, 21, 22, 41 are cancelled.

Claims 11-14, 20, 30, 33-36, 40, 42-52 are currently pending.

The previous claims rejection under 35 USC 103(a) set forth in paragraphs 2-4 of the office action mailed June 4, 2001 **is withdrawn** in view of Applicant's amendment (10/30/01) and the remarks contained therein.

However, Applicant's amendments necessitated the following new grounds of rejection.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Black et al., 5,457,116 or Dodge 5,552,417.

Black et al. disclose methods of inhibiting uterine fibrosis comprising administering effective amounts of a composition containing raloxifene which may be administered serially or concurrently with a gonadotropin releasing hormone antagonist. Moreover, raloxifene may formulated into sustained release compositions that release the raloxifene over a period of time. Please see col. 3, lines 31-57.

Dodge discloses methods of inhibiting sexual precocity comprising administering effective amounts of a composition containing raloxifene wherein the compositions may be formulated as sustained release compositions which release the raloxifene over a period of time. Dodge

additionally discloses that raloxifene may also be administered with a LHRH agonist. Please see col. 1, line 65 to col. 2, line 62.

Black et al. or Dodge do not specifically disclose pharmaceutical compositions containing a combination of raloxifene and the gonadotropin releasing hormone (GnRH) antagonist or the LHRH agonist; however, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Black and Dodge to combine the two components because Black and Dodge suggest that the administration of raloxifene with the GnRH antagonist or the LHRH agonist would aid in the treatment uterine fibrosis or sexual precocity. Thus, one of ordinary skill in the art would reasonably expect a pharmaceutical composition containing a combination of raloxifene and GnRH antagonist or a LHRH agonist to effectively treat patients suffering from uterine fibrosis or sexual precocity.

With respect to the specifically claimed LHRH analogs, in view of Black's and Dodge's teachings, it would have been obvious to one of ordinary skill in the art to use these conventionally known LHRH analogs with the reasoned expectation that they would be equally effective in treating uterine fibrosis and sexual precocity.

Finally, concerning the specifically claimed depot formulation, dosage forms and modes of administration are art-recognized result-effective variables and it would have been obvious to one of ordinary skill in the art to modify them in the prior art.

Claim Rejections - 35 USC § 112

4. Claims 51-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for raloxifene, does not reasonably provide enablement for all possible derivatives of raloxifene as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The claims are drawn to methods of inhibiting the detrimental side effects (bone loss) of LHRH analogs comprising administering an LHRH analog along with raloxifene or a derivative thereof.

(2) The state of the prior art

The art discloses raloxifene is a known anti-estrogen and that raloxifene is useful in a variety of treatment methods.

(3) The relative skill of those in the art

The relative skill of the those in the art is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical and chemical art is high.

(5) The breadth of the claims

The claims are very broad and encompass any derivative of raloxifene, known or yet undiscovered, that are or may be capable of inhibiting the bone reducing effects of LHRH analogs.

(6) The amount of direction or guidance presented

Applicant's specification provides guidance for and is only enabled for the use of raloxifene in the claimed methods. However, the specification provides no guidance, in the way of written description, to enable one of ordinary skill in the art to use the invention commensurate in scope with the claims. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims

are capable of accomplishing the desired result." Applicant's specification does not set forth a representative number of examples of raloxifene derivatives.

(7) The presence or absence of working examples

As stated above, the examples in Applicant's specification describe using raloxifene for inhibiting side effects of LHRH analogs. Therefore, the specification enables one of ordinary skill in the art to use raloxifene only in the claimed methods. The specification does not however, provide any examples of raloxifene derivatives that are useful in the claimed method.

(8) The quantity of experimentation necessary

Since the significance of compound structure and activity for pharmaceutical use must be determined from case to case by painstaking experimental study, one of ordinary skill in the art would be burdened with undue experimentation to determine which raloxifene derivatives would be capable of inhibiting LHRH analog induced bone loss.

Conclusion

Claims 48-50 and 51-52 are rejected.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is (703) 306-3227. The examiner can normally be reached on Tue-Fri from 8:30 to 6:00. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

CDM

Jan. 14, 2002

DWAYNE C. JONES
PRIMARY EXAMINER 1614